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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,536	03/03/2004	Lin Shiue Lian	8961-000010/US	3361
30593 7590 05/16/2007 HARNESSE, DICKEY & PIERCE, P.L.C. P.O. BOX 8910 RESTON, VA 20195			EXAMINER BERTOGLIO, VALARIE E	
			ART UNIT 1632	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/791,536

Applicant(s)

LIAN ET AL.

Examiner

Valarie Bertoglio

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 04/19/07.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03/03/04 and 07/02/04 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/19/2007 has been entered.

Claims 1,17 and 23 have been amended. Claims 1-24 are pending and under consideration in the instant office action.

Applicant requested, in their reply, to speak with the Examiner. An interview is summarized on the attached interview summary form.

Claim Objections

The objection to claim 23 is withdrawn.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for generating an ornamental fish comprising (a) generating a transgenic oviparous fish whose genome comprises one or more genes encoding a fluorescent protein operably linked to a promoter, wherein the transgene is expressed in the fish; (b) breeding the transgenic fish with a fish of the same or different species of the same genus having a phenotype or pattern that differs from the transgenic fish; and (c) screening the resulting transgenic progeny for those showing a

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phenotype or pattern that differs from each parent and fish made by said method, does not reasonably provide enablement for the claimed method with a transgenic viviparous fish or for mating fish across genera or family. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is maintained, in part, for reasons of record set forth at pages 2-6 of the previous office action dated 07/03/2006 as outlined below.

Applicant has amended the preamble of claim 1 to read "adult oviparous teleost ornamental fish" however, the method steps differ in scope and fail to limit the species of fish to oviparous species. Thus, the claims continue to encompass use of viviparous fish species, which is not enabled by the specification as set forth at pages 4-5 of the office action dated 07/03/2006. It appears to be Applicant's intention to limit the scope of the claim appropriately and adding the limitation to the body of claim 1 will be remedial for this aspect of the rejection. This aspect of the rejection is withdrawn for claim 17 as it has been amended and no longer recited Egg Laying Toothcarps.

The claims are also broad in encompassing mating transgenic fish of one species to fish of another species of different and divergent genera and families (see claim 3). It is noted that recitation of use of different species encompasses mating fish of different orders, family and genera.

The art at the time of filing held that while interspecies matings within a genus can often occur and can also be desired, matings of distantly related species of the same genus as well as matings of fish between different genera and families are highly unpredictable as to the success of the fertilization, development, health of any progeny that do occur and fertility of offspring. Bartley *et al.* discuss the use of inter-specific hybrids in aquaculture. Hybridization between species often results in offspring that are sterile or with diminished reproductive capacity as a result of problems in gonad development and chromosome pairing (paragraph bridging columns at page 330). The results of inter-specific hybridization can lead to unexpected and undesirable results and can depend on the genetic structure of the parent fish

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(Abstract). While inter-specific mating of certain species is known to result in various, desirable outcomes, these combinations are not easily arrived at, as evidenced by the mating of various species of grouper (page 332, col. 2, paragraph 2). With greater the divergence between two species comes increased divergence in chromosome number, pairing and compatibility of gene products.

The specification fails to set forth, of the many families of fish, which species of fish would provide valuable hybrid offspring. For example, the specification fails to support that transgenic zebrafish could mate or produce progeny by in vitro fertilization with any other fish encompassed by the claims such as tilapia, carp or salmon.

Thus, the specification fails to provide the guidance necessary to overcome the unpredictability in the art relating to mating fish of divergent species. It would require undue experimentation to determine successful hybrid species using matings between fish of different genera.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

Claim 1 remains unclear at step (c) because it does not recite what is to be screened. The claim previously read, "screening the new transgenic progeny". As amended the claim reads "screening for new transgenic progeny" without setting forth what group is to be screened. Language such as "screening the transgenic progeny for those exhibiting..." would be clearer. Claims 2-24 depend from claim 1. Applicant has not addressed this aspect of the rejection.

Claim 1 is further unclear because the preamble, as amended, requires that an adult fish be made, however, the methods steps fail to make such a requirement. The method steps merely require screening progeny and do not require growth to an adult fish. Thus, the claim is not clearly limited to making an adult fish as indicated by Applicant at page 9, paragraphs 1 and 2 of Applicant's Remarks dated 10/03/2006. Claims 2-24 depend from claim 1. Applicant has not addressed this aspect of the rejection.

The rejection of claim 17 is withdrawn because it no longer recites a viviparous species of fish, Livebearing toothcarp.

Claim 1 is unclear as amended because it is not clear if the α -actin or β -actin promoter is part of the claimed transgene or is an endogenous promoter or part of some other exogenous DNA. More clear language would include "the genome of the transgenic fish comprises a transgene comprising a gene encoding a fluorescent product operably linked to the α -actin or β -actin promoter". Claims 2-24 depend from claim 1.

Claim 23 recites the limitation "The ornamental fish" in line 1. There is insufficient antecedent basis for this limitation in the claim. Use of "An ornamental fish" would be appropriate because claim 1 is drawn to making a progeny fish, not fish prepared from the progeny as in claim 23. Use of the term "The" in the instant claim indicates that the fish is that made in claim 1. However, claim 23 is drawn to a fish that is a progeny of the fish made in claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1,2,5-9 and 23 under 35 U.S.C. 102(a) as being anticipated by Lawson and Weinstein is withdrawn in light of Applicant's amendment to claim requiring the use of the α -actin or β -actin promoter.

The rejection of claims 1,2,5-9 and 23 under 35 U.S.C. 102(a) as being anticipated by Fadool is withdrawn in light of Applicant's amendment to claim requiring the use of the α -actin or β -actin promoter.

Claims 1,2,5-9 and 23 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Higashijima [**Developmental Biology**, 1997, 192:289-299].

Claims 1 and 2 are drawn to a method of making a fish comprising steps of generating a transgenic fish, breeding said fish to a second fish that has a different phenotype or pattern and screening the transgenic progenies for those exhibiting a phenotype or pattern that differs from either of the parents. Claim 5 limits claim 1 to use of a number of specific fluorescent protein encoding genes including EGFP. Claim 6 and 7 limit claim 1 to a smaller number of specific fluorescent protein encoding genes, each including GFP and EGFP. Claims 8 and 9 limit the phenotype to certain observable morphological phenotypes including body transparency. Claim 23 is limited to the fish made by the method of claim 1. Claim 1 recites a limitation in the preamble that the fish be an adult, however, as set forth above in the rejection under 35 USC 112, 2nd paragraph, the method steps of the claims fail to require any methodology that leads to an adult fish. However, for the purpose of this rejection, the claim is interpreted generically as though it encompasses adult and non-adult fish.

Higashijima taught generating a transgenic fish comprising a transgene comprising a gene encoding a fluorescent protein (EGFP) operably linked to either the α -actin or β -actin promoters and breeding the progeny to wildtype zebrafish (page 297, paragraph 1). The wild-type fish mated to the

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transgenic fish differs in phenotype and pattern because the wildtype fish lacks fluorescence that is present in the phenotype and pattern of the transgenic fish.

Therefore, Higashijima taught the limitations of claims 1,2,5-9 and 23.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1,2,5-9 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Higashijima [Developmental Biology, 1997, 192:289-299] in view of Lawson and Weinstein [Developmental Biology, 248:307-318, of record].

The above set forth rejection under 35 USC 102 (b) is applied under 35 USC 103(a) to the extent that the claim reads on breeding the transgenic fish to a fish with a different phenotype or pattern other than the difference caused by introduction of the transgene.

Higashijima taught generating a transgenic fish comprising a transgene comprising a gene encoding a fluorescent protein (EGFP) operably linked to either the α -actin or β -actin promoters and breeding the progeny to wildtype zebrafish (page 297, paragraph 1). Higashijima did not teach breeding the transgenic fish to fish of a different phenotype or pattern other than that caused by the transgene.

However, Lawson and Weinstein taught generating a transgenic GFP expressing zebrafish using wild-type, pigmented (EK; page 310, col. 1, paragraph 3) *Danio rerio* (*Brachydanio rerio*). The transgenic fish was mated to an unpigmented albino mutant of the same species, resulting in a transgenic GFP, albino mutant. For example, see Figure 5 and legend. Albino mutants have an altered body transparent level as a result of a loss of pigmentation.

It would have been obvious at the time the application was filed to combine the teachings of Higashijima in making a transgenic fish exhibiting stable and reproducible fluorescent reporter gene expression with those of Lawson and Weinstein to mate the transgene of Higashijima into an albino mutant fish. One of skill in the art would have been so motivated to obtain a fish exhibiting a fluorescent pattern that is not obscured by the natural pigment pattern of the fish.

One would have a reasonable expectation of success in carrying out the combination because albino mutant zebrafish will readily mate with other zebrafish.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Higashijima [Developmental Biology, 1997, 192:289-299] in view of Bartley *et al* [Reviews in Fish Biology and Fisheries, 2001, 10:325-337] taken with Gong et al [Genetica, 111:213-225, 2001].

Higashijima taught generating a transgenic fish comprising a transgene comprising a gene encoding a fluorescent protein (EGFP) operably linked to either the α -actin or β -actin promoters and breeding the progeny to wildtype zebrafish (page 297, paragraph 1). Higashijima did not teach breeding the transgenic fish to fish of a different species.

However, Bartley *et al.* taught that there are many different species of fish that can interbreed to form hybrid species and that hybrid species often can lead to more desirable traits including a variety of traits that make fish more profitable to raise (see paragraph bridging columns at page 326) or that result in alterations in morphology (phenotype).

Furthermore, Gong et al taught the use of transgenic fluorescent protein expressing fish as having ornamental value (see page 222).

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It would have been obvious at the time the application was filed to combine the teachings of Higashijima in making a transgenic fish exhibiting stable and reproducible fluorescent reporter gene expression with those of Bartley to mate the transgene of Higashijima into a fish of different species to create fish with a combination of parental traits. One of skill in the art would have been so motivated to obtain such a fish because Gong *et al* pointed out the use of fluorescent fish as having ornamental value and interspecies crosses would supply an already integrated and expressed transgene to fish of different morphologies.

One would have a reasonable expectation of success in carrying out the combination because interspecies mating of certain closely related fish was known and routine in the art.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

Applicant is advised that should claim 3 be found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 4 does not appear to differ in scope from claim 3. While claim 4 fails to recite that the fish be from different family or genus, by reciting different species in claim 4, the claim encompasses those of different genus and family as well. Claim 4 is not limited to different species of the same genus.

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Valarie Bertoglio
Primary Examiner
Art Unit 1632